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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,721	02/09/2004	Ralf Jockers	FRAV2003/0005USNP	9535
5487 7590 08/16/2007 ANDREA Q. RYAN SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			EXAMINER WOLLENBERGER, LOUIS V	
			ART UNIT 1635	PAPER NUMBER
			NOTIFICATION DATE 08/16/2007	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/774,721

Applicant(s)

JOCKERS ET AL.

Examiner

Louis V. Wollenberger

Art Unit

1635

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 07 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 07 August 2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 12-15, 17, 47 and 48.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_  
13. ☐ Other: \_\_\_\_\_.

Continuation of 5. Applicant's reply has overcome the following rejection(s): The rejections of record under 35 USC §112, first and second paragraphs, would be withdrawn in view of Applicants' amendments to the claims. .

Continuation of 11. does NOT place the application in condition for allowance because: For purposes of appeal, the proposed amendment(s) will be entered and the proposed rejection(s) detailed below will be included in the Examiner's Answer. To be complete, such rejection(s) must be addressed in any brief on appeal.

Upon entry of the amendment(s) for purposes of appeal:

Claim(s) 12-15, 17, 47, and 48 would be rejected for the reasons set forth in the Office Action mailed 9/7/2005 (pages 8-14), as updated in the Non-Final Action mailed 6/28/06 (pages 14-18), and as reiterated in the final action (pages 9-13) mailed 2/9/07.

Applicants' amendment to claim 15 overcomes the objection to claims 15 and 48 for improper multiple dependency. Accordingly, with entry of the amendment, claims 15 and 48 would be included in the rejection under 35 USC §103 now of record.

With regard to claims 15 and 48, as presented in the After-Final Amendment of 8/7/07, Bailleul et al. taught art-recognized methods for expressing antisense molecules from vectors and methods for introducing said vectors into cells (paragraphs 128- 138). For example, at paragraph 136 it is taught that "... antisense cDNA constructs that synthesize antisense RNA constitutively or inducibly can be introduced into cell lines, cells or tissues", as explained at page 9 of the Action mailed 9/7/05.

Applicant's arguments filed 8/7/07, with regard to the Final Rejection of claims 12-14, 16, 17, 45, and 47, have been fully considered but are not persuasive.

Claims 16 and 45 are no longer pending.

As regards claims 12-14, 17, and 47, Applicants argue the references do not teach all the claimed limitations inasmuch as the references do not teach interfering RNA. In particular, Applicants argue that Agrawal et al. did not teach that antisense oligonucleotides could be RNA. Applicants argue RNA is discussed only in the context of ribozymes and that the examples of hairpin antisense oligonucleotides described by Agrawal et al. are drawn to DNA not RNA. Therefore, Applicants assert, adaptation of these examples to oligoribonucleotides is not taught or suggested by the applied references.

Applicants' arguments are not persuasive because Agrawal et al. is not limited to the examples, but includes all that it taught and/or reasonably suggested to one of skill at the time of invention.

In this regard, Agrawal et al. taught that self-stabilized antisense oligonucleotides of their invention can comprise RNA, DNA, or both RNA and DNA nucleotides. See especially page 8, lines 9-15 and page 16, lines 5-23. Both Rnase H-activating embodiments and non-RNase H embodiments (page 16, lines 20-23) are taught, embracing both partial and fully RNA molecules. To this extent, and to the extent Agrawal et al. taught that self-stabilized antisense oligos are preferably from 8 to 50 nucleotides in length (pp. 9-10), Agrawal et al. taught interfering, double stranded RNA molecules within the scope of the instant claims. The claims embrace hairpin iRNA molecules wherein the sense and antisense strands are present in a single olionucleotide molecule. Neither the claims nor the specification specifically excludes iRNA oligonucleotides comprising one or more modified nucleotides, such as deoxyribonucleotides, nor specifically requires that each of the nucleotides in iRNAs be RNAs. Rather disclosure at page 9 of the specification (translation) indicates that iRNAs embrace modified and unmodified species. Applicants present no evidence that the self-stabilized antisense molecules taught or suggested by Agrawal et al. would be incapable of interfering with gene expression.

Further, Bailleul et al. taught that antisense molecules can be expressed intracellularly from a vector. Such molecules would necessarily be composed of RNA.

Claims 13, 14, 17, and 47 would remain objected to and claims 15 and 48 would be objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants' arguments on this point are not persuasive, since neither the claims nor the specification clearly define "double-stranded" as being limited to molecules consisting of two separate, non-covalently linked strands. For purposes of this examination, hairpin molecules are considered to be double stranded as they comprise a double helix consisting of two strands.

/Sean McGarry/  
Primary Examiner  
AU 1635